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09/578,693	05/26/2000	Masaya Yamanouchi	20-4710P	9841

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EXAMINER
COOK, LISA V

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1641	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/578,693	Applicant(s) YAMANOUCHI ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,6,7,9 and 14-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,6,7,9 and 14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6&8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's response to the Office Action mailed 10 April 2001 is acknowledged (paper #7 filed 9/14/01). In amendment-A filed therein the abstract, specification and claims 2, 4, 6, 7, 9, 14, 15 were amended. While new claims 16-23 were added.

2. Claims 2, 4, 6, 7, 9, and 14-23 are pending and currently under consideration.

OBJECTIONS WITHDRAWN

Priority

3 Applicants have amended the specification to include foreign application No. 9-323684 filed 11/26/97 in Japan. Foreign application No. 87119150 filed 11/19/98 in Taiwan was not included because applicant dos not claim priority to the cited application. The amendment has obviated the following objections:

A. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application does not contain the required first sentence of the specification referencing priority document foreign application No. 9-323684 filed 11/26/97 in Japan and foreign application No. 87119150 filed 11/19/98 in Taiwan. Please add to the specification. The objection is withdrawn.

B. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 9-323684, filed on 11/26/97. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action. The objection is withdrawn.

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Application No. 87119150 on 11/19/98. It is noted, however, that applicant has not filed a certified copy of the Taiwan application as required by 35 U.S.C. 119(b). The objection is withdrawn.

Specification

5. Applicants amendments to the disclosure have obviated the following objections:

A. The abstract of the disclosure is objected to because there appears to be a typo on line 8 wherein it recites "diagnosis of prognosis of". It is not clear if applicant intended to recite "diagnosis or prognosis of". See MPEP § 608.01(b). The objection is withdrawn.

B. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. For example "Method for examining kidney diseases by detecting the fatty acid protein α_{2U}-globulin". The objection is withdrawn.

C. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The objection is withdrawn.

D. The disclosure is objected to because of the following informalities: A typo appears on page 25, line 17. Nucleotide is misspelled "necleotide". . The objection is withdrawn.

E. The use of the trademarks has been noted in this application. (.i.e. Superdex -page 27, line 3 and Sephacryl-page 23, line 1). All trademarks in the disclosure should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. The objection is withdrawn.

OBJECTIONS MAINTAINED

Information Disclosure Statement

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 has cited the references they have not been considered.

7. The information disclosure statements filed 8/9/01-Paper#6 and 9/12/01-Paper#8 have been considered as to the merits prior to final action.

Drawings

8. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(2) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(i), three sets of drawings or photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Response to Arguments

Applicant is required to file a petition filed under 37 CFR 1.84(a)(2) or (b)(2) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(i). The objection is maintained.

REJECTIONS WITHDRAWN

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for detecting the fatty acid binding protein - α_{2U}–globulin, it does not reasonably provide enablement for any and all methods detecting any and all fatty acid binding proteins for any and all kidney disease detection. The claims, as written, read on any fatty acid binding protein capable of detecting any Kidney disease. *(claims 1and 10).*

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim to detect *any and all kidney diseases* employing *any and all* fatty acid binding proteins, wherein detection of any fatty acid protein expressed by the animal is indicative of kidney disease in the animal. The only protein taught in the disclosure is α_{2U}–globulin.

Response to Arguments

Applicants have amended the claims to recite liver-type fatty acid binding protein, therein obviating the rejection. The rejection is with drawn.

Claim Rejections

10. With respect to the claim rejections under 35 U.S.C. 102 and 35 U.S.C. 103, Applicant's argument that and liver-type binding protein are not the same have been found convincing. The following rejections are withdrawn:

I. Claims 1, 2, 4-8, 10, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536).

II. Claims 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Kimura et al. (Journal of Biological Chemistry, 3/25/91, Vol.266., No.9., pages 5963-5972).

III. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Galaske et al. (Pflugers Archives European Journal of Physiology, 1978, 375,3, 269-277-ABSTRACT ONLY).

IV. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102, 1990, pages 524-536) in view of Zuk et al. (U.S.Patent #4,281,061).

NEW GROUNDS OF REJECTION NECESSITAED BY AMENDMENT

Claim Objections

11. Claim 17 is objected to because of the following informalities: In line 3 "t" should be "to". Appropriate correction is required.

12. Claim 23 is objected to because of the following informalities: The claim does not end with a ".". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 20 provides for the use of the method of claim 16, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

14. Claims 7, 9, and 17 (including independent claim 16) are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

The claims are drawn to a method diagnosis or prognosis of kidney disease (in independent claim 16). The claims measure the presence of a live-type fatty acid binding protein–antibody complex in a sample of interest. However the claims do not include a separation step to remove unbound material. A method, as recited in the preamble of claim 16 further requiring antibody binding, requires at least a contact step between reagents and sample, a separation step, a detection step, and a There are no claimed steps reciting the washing or removal of unbound materials. If no separation will be performed it is unclear how the complex will be identified from the reaction solution (unbound material).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 7, 9, and 17 (including independent claim 16) are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The methods of claims 7, 9, and 17 have insufficient steps. These critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). There are no claimed steps reciting the washing/removal of unbound material.

A separation step that removes bound and unbound material from the detection complex involving a liver-type fatty acid binding protein antibody is missing. If you do not have a separation step after step (b), the addition of the fatty acid will always provide a positive result regardless of the bound/unbound reagents and thus could not be utilized to detect kidney disease. Please add the removal of unbound reagents to the claims or clearly indicate the specific method of detection that does not employ the removal of unbound material.

Response to Arguments

Applicant argues that the instant invention does not require a complex bound to fatty acid, therefore essential steps have not been omitted. This argument was carefully considered but not found persuasive because the claims require an antibody to bind liver-type fatty acid in a test sample. An antibody complex is required for detection and further requires separation of unbound material. The rejections cited in 13 and 14 above are maintained.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 2, 4, 6, 16, 17, 18, 20, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290).

Olson et al. disclose a comparative study evaluating α_{2U}–globulin protein concentrations in male rat and human (males aged 30-40 with no clinical signs of renal disease) urine samples. The disclosure teaches that α_{2U}–globulin protein is a fatty acid binding protein (FABP) synthesized in the liver and introduced into the urine from the kidney or kidney tissue. See page 4, lines 2-3, page 7, lines 10-15, and page 9, line 14. The urinary proteins were separated by chromatography and SDS-polyacrylamide gel electrophoresis.

Immunoidentification was accomplished via western blotting with polyclonal rabbit anti-rat α_{2U}-globulin antibody (page 526, 2nd column, 2nd paragraph) and biotinylated anti-IgG and avidin-horseradish peroxidase complex with 4-chloro-1-naphthol (page 526, 2nd column, 3rd paragraph). The fraction of α_{2U}-globulin protein in rat urine was 26% of the total urinary protein content and in humans the fraction was 4% of the total urinary protein content. High amounts of α_{2U}-globulin proteins were associated with hyaline droplet nephropathy (HDN). Page 525, 1st column, 2nd paragraph) This study suggested that humans were at no risk for the particular kidney disease - hydrocarbon-induced nephropathy.

Olson et al. differ from the instant invention in not specifically teaching the detection of liver-type fatty acid binding protein.

However, Maatman et al. identified the liver-type fatty acid binding protein utilized in the instant invention. Page 285, 1st column. This is supported by Applicants arguments (page 24 of the response filed 9/14/01 in paper #7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the liver-type fatty acid binding protein as taught by Maatmann et al., to detect the specific kidney diseases relating to FABP in the method of Olson et al. because Maatman et al. taught that "the liver-type FABP binds various ligands and may be involved in the renal excretion of exogenous and endogenous metabolites. The liver-type FABP also binds some drugs and may in this way prevent nephrotxicity". Page 289, 2nd column 1st paragraph.

II. Claims 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and further in view of Kimura et al. (Journal of Biological Chemistry, 3/25/91, Vol.266., No.9., pages 5963-5972).

See discussion of Olson et al. in view of Maatman et al. as set forth above.

Olson et al. differ from the instant invention in failing to teach that the liver-type FABP is found in the proximal tubule of the kidney and does not cross-react with a heart muscle-type fatty acid binding protein.

However, these characteristics of α_{2U}–globulin were already known in the prior art. Specifically Kimura et al. disclose that fatty acid-binding proteins found in the kidney could be distinguished according to their primary structure and histologic distribution. Two specific FABPs weighing 14 and 15.5 kDa were found in male rat kidney cytosol. The 14 kDa compound was identified as heart FABP and localized in the cytoplasm of the epithelia of the kidney distal tubules. The 15.5 kDa compound was identified as a proteolytically modified form of α_{2U}–globulin (alpha 2u-globulin) and localized in the endosomes or lysosomes of kidney proximal tubules.

Olson et al. in view of Maatman et al. and Kimura et al. are all analogous art because they are from the same field of endeavor, both inventions teach methods involving FABP detection.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the antibody which would not cross-react with a muscle-type fatty acid binding protein as taught by Kimura et al., to detect the specific kidney FABP in the method of Olson et al. in view of Maatman et al. because such antibodies as taught by Kimura et al. are well known in the art.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such antibody assays, because Kimura et al. had already taught that the kidney contained two different types of fatty acid binding proteins, one designated the heart-FABP and the other designated the kidney-FABP. (page 5964, Results).

One having ordinary skill in the art would have been motivated to distinguish between the two types by employing an antibody that would not cross react with the other type (heart-FABP/kidney distal tubules) in order to receive an accurate, more precise measure of the concentration of the FABP of interest (in this case kidney-FABP/ kidney proximal tubules).

III. Claims 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and further in view of Galaske et al. (Pflugers Archives European Journal of Physiology, 1978, 375,3, 269-277-ABSTRACT ONLY).

Please see previous discussions of Olson et al. in view of Maatman et al.

Olson et al. in view of Maatman et al. differ from the instant invention in not teaching a detection system involving a chronic renal disease (anti-GMB-nephritis model) further monitoring specimen collection at various intervals.

Galaske et al. disclosed the glomerular filtration and tubular uptake of plasma proteins in the acute heterologus phase of an anti-GMB nephritis model. Injections of anti-glomerular-basement membrane serum (anti-GMB-serum) were evaluated in tubular reabsorption and tubular flow at various times. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a anti-GMB nephritis model as taught by Galaske et al., to detect kidney diseases via proteins in the method of Olson et al. in view of Maatman et al. because Galaske et al. disclose that such models existed allowing for protein detection in plasma and urine.

One of ordinary skill in the art would have been motivated to do this in order to detect renal disorders at the onset and follow the disease progression/regression.

III. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102, 1990, pages 524-536) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and further in view of Zuk et al. (U.S.Patent #4,281,061).

The teachings of Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) are set forth above. Although the reference teaches reagents for examining kidney disease, the references fail to teach the assay as a kit.

However, Zuk et al. (4,281,061) teach that "as a matter of convenience the reagents [of an immunoassay} can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest" (column 22, lines 63-66).

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the kidney disease detection assay as taught by Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and format them into a kit because Zuk et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre measured amounts which eliminates the variability that can occur when performing the assay.

17. For reasons aforementioned, no claims are allowed.

Remarks

18. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Nagasawa (Japanese Med. Res. Found. Publ. 1979, 7 (Glomerulonephritis), pages 39-51)- ABSTRACT ONLY teach that the binding distribution of Con A is similar anti-nephritogenic glycoprotein antibody.

19. New grounds of rejection were presented in the Office Action. It is therefore made NON- **FINAL.** Examiner apologizes for any inconvenience this may cause Applicant.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
(703) 305-0808
5/31/02

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641